REMARKS

Claims 1-10 and 12-18 are pending. Applicants have cancelled claims 3 and 4 without prejudice. Claims 1, 2, 5-10, and 12-18 will therefore be pending upon entry of the proposed amendments.

Support for the amendment to claim 1 can be found throughout the specification, e.g., at page 8, lines 21-22.

Office's response to arguments presented in previous reply

The Office Action states, in part, on page 2 (emphasis added):

> The rejection for scope of enablement are maintained as the directions for the preparation and use of the compounds commensurate in scope with the claims has not been provided. The number of examples provided by the specification are few and have been discussed previously (and are reproduced here again vide infra). **It would appear that the applicant is arguing that essentially any molecule, even molecules of unknown structure, can be made without undue experimentation.**

Applicants wish to address the underlined portion of the above-quoted passage from the Office Action. Applicants did not take the position that "essentially **any** molecule, even molecules of **unknown** structure, can be made without undue experimentation" (Office Action, page 2, emphasis added). Rather, Applicants argued that a person of ordinary skill in the art, given the present specification as a guide and the ability to modestly experiment, could make and use the compounds encompassed by the present claims without undue experimentation. Further, since the skilled person could readily discern which chemical structures fall within the claimed genus and which do not, there are no "molecules of unknown structure" encompassed by the present claims.

Maintained Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-6 and 9 remain rejected for allegedly failing to comply with the enablement requirement of 35 U.S.C. § 112, first paragraph. The rejection includes a number and variety of supporting information, such as quotations from a recent treatises on organic synthesis and results of a search of the Aldrich Chemical Company catalog. Applicants will therefore begin by summarizing some of the points and information raised throughout the rejection.

[1] Brief Synopsis of Rejection

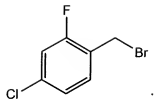
[A] The rejection begins by stating, in part (Office Action, page 11):

> [T]he specification, while being enabling for certain compounds, does not reasonably provide enablement for the protracted list of compounds bearing the protracted list of substituents. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make of use the invention commensurate in scope with these claims.

This statement is followed by a brief review of the so-called Wands (*In re Wands* 858 F.2d 731) factors.

[B] Next, the Office provides a composite reaction scheme (see Scheme 1 on page 14 of the Office Action), which apparently is intended to show the starting materials and intermediates used to prepare the title compound of Example 1 in the specification[1]. The Office then indicates that it conducted a search to determine whether some of these starting materials and intermediates were commercially available. It appears that this search was limited to a search of the Aldrich Chemical Company ("Aldrich") catalog. One of the starting materials that was searched was 2-(bromomethyl)-4-chloro-1-fluorobenzene, the structure of which is shown below:

[1] Applicants respectfully point out that compound **6** in Scheme 1 on page 14 of the Office Action should show the chemical structure of *p*-methoxybenzyl chloride rather than *p*-methoxybenzoyl chloride (i.e., the structure should not have a carbonyl group; see specification at page 28, lines 23-24).



According to the Office's search results, Aldrich does not, at the present time, appear to sell 2-(bromomethyl)-4-chloro-1-fluorobenzene.

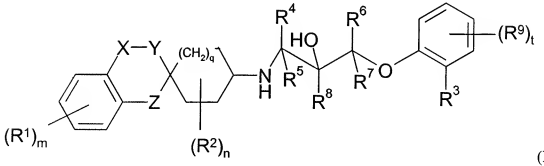
[C] The Office Action then goes on to state:

> If such starting materials could be obtained ... it is very clear that the protracted list of substituents for R^1 cannot undergo the synthetic procedures given. Nitriles and other electrophiles will also undergo addition by Grignards [citation omitted]. Metal halogen exchange between a ("halo") like iodine and a Grignard will also occur [citation omitted]. The "alkylhalo" compounds will undergo metal exchange when in the presence of a Grignard (Knochel ibid.).
>
> Another disturbing feature of what is before the examiner, is the fact that is appears that no assays were performed.

This is respectfully traversed.

[2] <u>The Claimed Compounds</u>

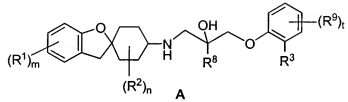
Claim 1 is directed to compounds having formula (I):



(I).

The claims in their present (and previously presented form) require that X must be a bond, Y must be -O-, Z must be $-CH_2$; q must be 1; and R^4, R^5, R^6, R^7 must each be a hydrogen atom.

As such, the claimed compounds are required to have the following core structure (referred to throughout as formula (A)):



A

For the convenience of the Office, the remaining permitted points of variability on the core structure are set forth below:

m is 0, 1, 2, 3 or 4;

each R^1 independently represents halogen, cyano, hydroxyl, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy or sulphonamido;

n is 0, 1 or 2;

each R^2 independently represents halogen or C_1-C_6 alkyl;

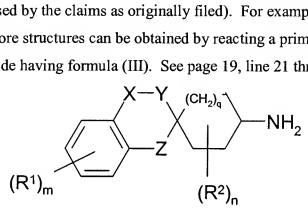
R^3 represents $-NHC(O)R^{10}$, $-C(O)NR^{11}R^{12}$ or $-COOR^{12a}$;

R^8 represents a hydrogen or C_1-C_6 alkyl group;

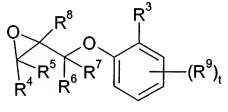
t is 0, 1 or 2; and

each R^9 independently represents halogen, cyano, hydroxyl, carboxyl, C_1-C_6 alkoxy, C_1-C_6 alkoxycarbonyl, C_1-C_6 haloalkyl, or C_1-C_6 alkyl optionally substituted by at least one substituent selected from carboxyl and C_1-C_6 alkoxycarbonyl."

[3] The specification at page 19, line 18 through page 22, line 14 provides various processes for synthesizing the core structure required by the present claims (as well as the other core structures encompassed by the claims as originally filed). For example, the specification teaches that the claimed core structures can be obtained by reacting a primary amine having formula (II) with an epoxide having formula (III). See page 19, line 21 through page 20, line 3.



(II)



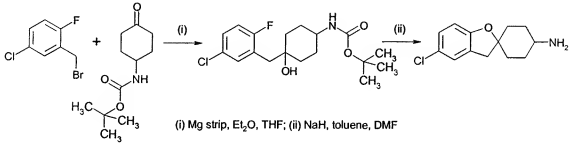
(III)

As another example, the claimed core structures can also be obtained, e.g., by reacting an epoxide of formula (IV) with a phenol of formula (V) (formulas not shown, see specification at page 20, lines 4-8). As a further example, a process is taught for installing an amide or reverse amide (i.e., the substituent corresponding to R^3) on the right most phenyl ring in formulas (I) and (A) (see specification at page 20, line 9 through page 21, line 12).

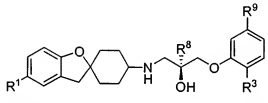
The specification goes on to disclose that the starting materials and other reagents were, as of Applicants' filing date, "commercially available, known in the literature, or may be prepared using known techniques" (specification at page 22, lines 2-3). In addition, detailed synthesis information (solvents, reagents, reaction temperatures, use of protecting groups) for the process steps is also provided. See specification at page 21, line 17 through page 22, line 3.

There is ample disclosure showing that the processes and guidance described above can be applied to the synthesis of compounds having the core structure required by the present claims. See, for example, the working example beginning at page 27, line 4, which shows the

synthesis of a representative amine of formula (II) from a commercially available benzyl bromide and a commercially available cyclohexanone:



See also Examples 1-5, which describe the synthesis of the following compounds:



Example	R^1	R^3	R^8	R^9
1	Cl	-C(O)NHMe	H	OH
2	Cl	NHAc	H	F
3	Cl	-C(O)NHMe	H	H
4	Cl	NHAc	H	OH
5	Cl	NHAc	Me	OH

As such, a person of ordinary skill in the art, using the knowledge he or she has, using the tools of chemistry, and guided by the Specification, could make the claimed compounds without undue experimentation.

[4] Before addressing the present rejection, Applicants first wish to discuss some of the relevant case law pertaining to the enablement requirement of 35 U.S.C. § 112, first paragraph.

35 U.S.C. § 112, first paragraph provides in relevant part:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, …

I. The law does not require that every species of a genus be shown by a working example (even in the so-called unpredictable arts). To require this would limit the Applicant merely to what he or she has already done.

A. In fact, the Court of Customs and Patent Appeals (CCPA) in *In re Robins* 166 USPQ 552, 555 (1970) held that disclosure of representative compounds of a claimed genus is not even a requirement of § 112 (emphasis in original):

> Both the examiner and the board seem to have taken the position that in order to 'justify,' as the examiner said, or to 'support,' as the board said, broad generic language in a claim, the specification must be equally broad in its naming, and use in examples, of representative compounds encompassed by the claim language. This position, however, misapprehends the proper function of such disclosure. Mention of representative compounds encompassed by generic claim language clearly is not required by § 112 or any other provision of the statute. ... [R]epresentative examples are not required by the statute and are not an end in themselves. Rather they are a *means* by which certain requirements of the statute may be satisfied.

B. The CCPA in *In re Angstadt and Griffin* 190 U.S.P.Q. 214, 218 (1976) held that (emphasis in original) " appellants are *not* required to disclose *every* species encompassed by their claims even in an unpredictable art." As the Court explained (*Id.* at 218, italic emphasis in original; bolded underline emphasis added):

> Appellants have apparently not disclosed *every* catalyst which will work; they have apparently not disclosed *every* catalyst which will not work. The question, then, is whether in an unpredictable art, section 112 requires disclosure of a test with *every* species covered by a claim. To require such a complete disclosure would apparently necessitate a patent application or applications with 'thousands'[2] of examples or the disclosure of 'thousands' of catalysts along with information as to whether each exhibits catalytic behavior resulting in the production of hydroperoxides. More importantly, such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments. **This would tend to discourage inventors from filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments which are expressly disclosed**. A potential infringer could readily avoid 'literal' infringement of such claims by merely finding another analogous catalyst complex which could be used in 'forming hydroperoxides.'

In *Angstadt*, the appealed claims were directed to methods of catalytically oxidizing secondary or tertiary alkylaromatic hydrocarbons to form the corresponding hydroperoxides. *Angstadt's* methods included contacting the hydrocarbon with a complex catalyst consisting of a transition metal salt and a phosphoramide. The Court noted that *Angstadt's* application disclosed "a large but finite list of transition metal salts" (*Id.*), but also pointed out that "Appellants have actually carried out 40 runs using various transition metal salts and hexaalkyl-phosphoramides" (*Id.*). The Court concluded (*Id.*):

> If one skilled in this art wished to make and use a transition metal salt other than those disclosed in appellants' 40 runs, he would merely read appellants' specification for directions how to make and use the catalyst complex to oxidize the alkylaromatic hydrocarbons, and could then determine whether hydroperoxides are, in fact, formed. The process discovered by appellants is not complicated, and there is no indication that special equipment or unusual reaction conditions must be provided when practicing the invention. One skilled in this art would merely have to substitute the correct mass of a transition metal salt for the transition metal salts disclosed in appellants' 40 runs. Thus, we have no basis for concluding that persons skilled in this art, armed with the specification and its 40 working examples, would not easily be able to determine which catalyst

complexes within the scope of the claims work to produce hydroperoxides and which do not.

It is further noted that the Court arrived at this conclusion even in view of the fact that "one of these examples yields no hydroperoxides in the final product. Also, appellants have expressly indicated in their specification that some of these organometallic complex catalysts 'yield * * * no hydroperoxides in the final product'" (*Id.*).

See also *Regents of University of California v. Eli Lilly & Co.* 43 USPQ2d 1398, 1406 (Fed. Cir. 1997) (underline emphasis added):

> This is analogous to enablement of a genus under § 112, ¶ 1, **by showing the enablement of a representative number of species within the genus**. See *Angstadt*, 537 F.2d at 502-03, 190 USPQ at 218 (deciding that applicants "are not required to disclose every species encompassed by their claims even in an unpredictable art" and that the disclosure of forty working examples sufficiently described subject matter of claims directed to a generic process);

In general, one can rely on the disclosure of representative compounds to satisfy the enablement requirement of § 112, first paragraph for a claimed genus. However, even in the unpredictable arts, one need not disclose every species encompassed by a genus to enable a claim to that genus.

II. "Patents are written by and for skilled artisans"[2]

A. The Federal Circuit discussed the enablement requirement of 35 U.S.C. § 112, ¶1 in *In re Buchner* 18 USPQ2d 1331, 1332 (1991) (bolded underline emphasis added, italics in original):

> In order to be enabling under 35 U.S.C. § 112, a patent application must sufficiently disclose an invention to enable those skilled in the art to make and use it. **The specification need not disclose what is well known in the art**. *Lindemann Maschinenfabrik GMBH v. American Hoist and Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

[2] *See Vivid Technologies, Inc. v. American Science and Engineering, Inc.*, 200 F.3d 795, 804, 53 USPQ2d 1289, 1295 (Fed. Cir. 1999).

The quote in *Buchner* later points out that an applicant is permitted, under the provisions of the statute, to exclude from his or her Specification information that is known in the art.

Accordingly, the fact that the specification does not disclose certain information, does not make a disclosure non-enabling. Evidentiary weight must be given to what was known in the art as of the applicants' filing date.

B. Subsequent to *Buchner*, the Federal Circuit, in *AK Steel v. Sollac* 68 USPQ2d 1280, 1287 (Fed. Cir. 2003)(emphasis added), considered the requirements for an enabling disclosure in view of *In re Wands* 8 USPQ2d 1400 (Fed. Cir. 1988), which is relied upon by the Examiner in the 35 U.S.C. § 112, first paragraph rejections of record:

> The enablement requirement is satisfied when one skilled in the art, after reading the specification, could practice the claimed invention without undue experimentation. *Wands*, 858 F.2d at 736-37. ... **That is not to say that the specification itself must necessarily describe how to make and use every possible variant of the claimed invention, for the artisan's knowledge of the prior art and routine experimentation can often fill gaps**, interpolate between embodiments, and perhaps even extrapolate beyond the disclosed embodiments, depending on the predictability of the art. *See Genentech, Inc. v. Nordisk A/S*, 108 F.3d 1361, 1366 [42 USPQ2d 1001] (Fed. Cir. 1997) ('[A] specification need not disclose what is well known in the art.'); see also *Wands*, 858 F.2d at 736-37 ('Enablement is not precluded by some experimentation, such as routine screening'). ... The question more precisely here is whether, with AK Steel's patent specification as an initial guide, the hypothetical skilled artisan's knowledge of the surrounding art and ability to modestly experiment would have been sufficient to enable him to make and use a steel strip containing a Type 1 aluminum coating, with the claimed wetting attributes at the time of the '549 patent's effective filing date in 1986 (*AK Steel* at 1287).

See also, *Amgen Inc. v. Hoechst Marion Roussel Inc.* 65 USPQ2d 1385, 1400 (Fed. Cir. 2003) (emphasis added), where the Court reasoned:

> The specification need **not** explicitly teach those in the art to make and use the invention; **the requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without 'undue experimentation'** *[citations omitted]*.

Accordingly, the fact that a Specification does not disclose certain information does not make a disclosure non-enabling. Rather, the enablement inquiry must focus on whether a person

of ordinary skill in the art, given his or her knowledge of the prior art and the ability to modestly experiment, could bridge any gaps between the breadth of the disclosure and the breadth of the claims.

C. See also, *S3 Inc. v. nVIDIA Corp.* 59 USPQ2d 1745, 1749-50, (2001), where the Federal Circuit explained (bolded underline emphasis added):

> The law is clear that patent documents need not include subject matter that is known in the field of the invention and is in the prior art, for patents are written for persons experienced in the field of the invention. *See Vivid Technologies, Inc. v. American Science and Engineering, Inc.*, 200 F.3d 795, 804, 53 USPQ2d 1289, 1295 (Fed. Cir. 1999) (**'patents are written by and for skilled artisans'). To hold otherwise would require every patent document to include a technical treatise for the unskilled reader**.

III. Enablement is not precluded by experimentation as long as it is routine experimentation and not undue experimentation.

A. The Federal Circuit discussed the "purpose" of the enablement provision in *Scripps Clinic & Research Foundation v. Genentech, Inc.* 18 USPQ2d 1001, 1006 (2001):

> The purpose of this provision is to assure that the inventor provides sufficient information about the claimed invention that a person of skill in the field of the invention can make and use it without undue experimentation, relying on the patent specification and the knowledge in the art.

See also the Federal Circuit's discussion of the purpose of the enablement requirement in *Warner-Lambert Co. v. Teva Pharmaceuticals USA, Inc.* 418 F.3d 1326, 1336-1337 (2005) (underline emphasis added):

> The purpose of this requirement is to ensure that 'the public knowledge is enriched by the patent specification to a degree **at least commensurate with the scope of the claims**.' *Nat'l Recovery Techs., Inc. v. Magnetic Separation Sys., Inc.*, 166 F.3d 1190, 1195-96 (Fed.Cir.1999); see also Donald S. Chisum, 3 Chisum on Patents § 7.01 (2002).

The Federal Circuit in *Warner-Lambert* stressed that the specification must teach one how to make and use the claimed invention without undue experimentation (*Id.* at 1337, emphasis added):

> Accordingly, we have held that the specification must provide sufficient teaching such that one skilled in the art could make and use the full scope of the invention without undue experimentation. *[citations omitted]* 'The key word is 'undue,' not experimentation." *Wands*, 858 F.2d at 737 (citation omitted). **That is, the specification need only teach those aspects of the invention that one skilled in the art could not figure out without undue experimentation**. See, e.g., *Nat'l Recovery Techs.*, 166 F.3d at 1196 ('The scope of enablement ... is that which is disclosed in the specification plus the scope of what would be known to one of ordinary skill in the art without undue experimentation.'); *Wands*, 858 F.2d at 736-37 ('Enablement is not precluded by the necessity for some experimentation such as routine screening.').

It is well settled that enablement is not precluded by experimentation. In other words, the enablement inquiry does not turn on whether experimentation may be needed to practice the claimed invention. Rather, the enablement inquiry turns on whether the amount of experimentation needed to practice the claimed invention is undue. *See, e.g., In re Angstadt and Griffin*, 190 USPQ 219 ("The key word is 'undue' and not 'experimentation.'").

B. The amount of experimentation can even be considerable, provided that it is routine and not undue. *See, e.g., Johns Hopkins University v. Cellpro, Inc.* 47 USPQ2d 1705, 1719 (Fed. Cir. 1998):

> Such routine experimentation does not constitute undue experimentation: 'The test [for undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention.' *[citations omitted]*.

See also, e.g., In re Wands 8 USPQ2d 1400, 1404 (Fed. Cir. 1988, emphasis added) ('Enablement is not precluded by some experimentation, such as **routine screening**').

[5] The Federal Circuit in *In re Wright* 27 USPQ2d 1510, 1513 (1993) discussed the requirements for rejecting a claim under the enablement requirement of 35 U.S.C. § 112, first paragraph:

> When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application; this includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement.

Applicants submit that the Office has not met this burden for any of the following independent reasons.

[6] The rejection appears to ignore the fact that the enablement inquiry **must** focus on whether a person of ordinary skill in the art, **given his or her knowledge of the prior art and the ability to modestly experiment**, could bridge any gaps between the breadth of the disclosure and the breadth of the claims.

[A] The present claims are directed to compounds that all share common and substantial structural attributes-- they are all required to have the same core structure (see formula (A) *supra*), and the specification provides ample guidance and direction for making this core structure and hence the claimed compounds (*vide supra*).

The Office's apparent concern regarding the (commercial) availability of 2-(bromomethyl)-4-chloro-1-fluorobenzene from Aldrich ("[m]ost disturbingly, we do not find the 5-chloro derivative which is required to synthesize all of the compounds that were actually made." Office Action, page 18) is misplaced for any one of the following independent reasons.

First, there is no legal requirement (or requirement in the specification or claims) that the claimed compounds must be made from commercially available starting materials.

Second, the compound in question was indeed commercially available as of Applicants' filing date.

Third, the Office's search was limited to only **one** vendor (Aldrich). The fact that the compound in question was not available from Aldrich would not have led the skilled artisan to reasonably conclude that the compound was not commercially available (or otherwise

unavailable by other means, such as conventional organic synthesis). In fact, Applicants were able to locate eleven current commercial suppliers of 2-(bromomethyl)-4-chloro-1-fluorobenzene by searching the ChemACX database provided by CambridgeSoft.

Finally, according to the Office, Aldrich does in fact sell (at least) fourteen 2-(bromomethyl)-1-fluorobenzenes that could be used to prepare some of the claimed compounds (see the chemical structures delineated on pages 15-18 of the Office Action). Thus, if anything, the Office's search results weigh on the side of Applicants' disclosure being enabling.

[B] Applicants now turn to the Office's comments summarized in paragraph **[1], [C]** above, namely:

> If such starting materials could be obtained ... it is very clear that the protracted list of substituents for R^1 cannot undergo the synthetic procedures given. Nitriles and other electrophiles will also undergo addition by Grignards [citation omitted]. Metal halogen exchange between a ("halo") like iodine and a Grignard will also occur [citation omitted]. The "alkylhalo" compounds will undergo metal exchange when in the presence of a Grignard (Knochel ibid.).
>
> Another disturbing feature of what is before the examiner, is the fact that is appears that no assays were performed.

The specification states that "certain protecting groups ... may need to be protected by protecting groups" (specification at page 22, lines 5-13). The skilled artisan would recognize that the issues raised above (if in fact they presented themselves) could be addressed, for example, by the use of protecting groups as taught by the specification. The skilled artisan would also recognize that a desired functional group could also be introduced at a different stage in the synthesis so as to avoid being exposed to potentially incompatible reaction conditions. Protection and deprotection of functional groups and functional group manipulation were within with the skill of the art as of Applicants' filing date and, at most, fall within the purview of routine experimentation, which does **not** preclude patentability. Moreover, The fact that the specification does not disclose such known (and arguably well known) methods and materials does **not** make Applicants' disclosure non-enabling. *See S3 Inc. v. nVIDIA Corp.* 59 USPQ2d 1745, 1749-50, (2001):

('[P]atents are written by and for skilled artisans'). To hold otherwise would require every patent document to include a technical treatise for the unskilled reader.

That being said, even if one or more of the claimed compounds could not be prepared (and Applicants do not concede that this is the case here), that does not render the claims unpatentable. The claims need not exclude inoperative embodiments. As the Federal Circuit explained in *Atlas Powder Co. v. E. I. Du Pont De Nemours & Co.* 224 USPQ 409 (Fed. Cir. 1984):

> Even if some of the claimed combinations were inoperative, the claims are not necessarily invalid. 'It is not a function of the claims to specifically exclude ... possible inoperative substances..." *Atlas Powder* at 414.

Finally, there is no legal requirement that the specification include biological data for the claimed compounds (in fact, there is no legal requirement that the specification provide working examples at all).

[7] The Office also appears to have taken the position that Applicants have enabled only those compounds that they have expressly disclosed and reduced to practice. This is evidenced by the above-quoted passages from the present Office Action, e.g., at page 11:

> [T]he specification, while being enabling for certain compounds, does not reasonably provide enablement for the protracted list of compounds bearing the protracted list of substituents.

This is respectfully traversed. First, as discussed elsewhere, to enable a claim to a genus, one need **not** disclose and test every species encompassed by the genus, even in the so-called unpredictable arts. To require as such would limit the Applicants merely to what he or she has already done. Again, this is not the law. *See, e.g., In re Angstadt*, 190 USPQ 214, (CCPA 1976). See also MPEP § 2164.02: "[b]ut because only an enabling disclosure is required, applicant need not describe all actual embodiments." Put simply, the law provides that one can enable a genus under § 112, ¶ 1, by showing the enablement of a representative number of species within the genus.

Finally, the enablement requirement also serves to advance the art to which the invention pertains. Applicants have provided the art with, *inter alia*, the knowledge that the claimed compounds modulate chemokine receptor activity. How is the art significantly or even incrementally benefited by requiring the Applicants to make and test additional compounds? Again, to require as such is effectively restricting the Applicants to claim only what they have done. This is unreasonable and is certainly not the law.

In summary, a person of ordinary skill in the art, using the knowledge he or she has, using the tools of chemistry, and guided by the Specification, could make the claimed compounds without undue experimentation.

In view of the foregoing, Applicants respectfully request that the 35 U.S.C. § 112, first paragraph rejection be reconsidered and withdrawn.

Rejections on the ground of nonstatutory obviousness-type double patenting

[1] Claims 1-7 and 9 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 and 10 of USSN 10/579,545 "in view of Xue et al. U.S. Pre-Grant Publication 2006/0252751" (Office Action, page 5).

Claims 1-7 and 9 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 and 12 of USSN 10/581,171 "in view of Xue et al. U.S. Pre-Grant Publication 2006/0252751" (Office Action, page 9).

Claims 1-7 and 9 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10, 12, and 14 of USSN 10/583,468 "in view of Xue et al. U.S. Pre-Grant Publication 2006/0252751" (Office Action, page 9).

Claims 1-7 and 9 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 and 13 of USSN 10/520,699 "in view of Xue et al. U.S. Pre-Grant Publication 2006/0252751" (Office Action, pages 9-10).

This is respectfully traversed.

[2] The Federal Circuit discussed the requirements for establishing a *prima facie* case of obviousness for a claimed chemical compound in *Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd.* 492 F.3d 1350, 135x (emphasis added):

> Our case law concerning prima facie obviousness of structurally similar compounds is well-established. We have held that "structural similarity between claimed and prior art subject matter, proved by combining references or otherwise, where the prior art gives reason or motivation to make the claimed compositions, creates a prima facie case of obviousness." *Dillon*, 919 F.2d at 692. In addition to structural similarity between the compounds, a prima facie case of obviousness also requires a showing of "adequate support in the prior art" for the change in structure. *In re Grabiak*, 769 F.2d 729, 731-32 (Fed.Cir.1985).
>
> We elaborated on this requirement in the case of *In re Deuel*, 51 F.3d 1552, 1558 (Fed.Cir.1995), where we stated that "[n]ormally a prima facie case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound." That is so because close or established "[s]tructural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds." *Id.* A known compound may suggest its homolog, analog, or isomer because such compounds "often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties." *Id.* We clarified, however, that in order to find a prima facie case of unpatentability in such instances, a showing that the "prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention" was also required. *Id.* (citing *In re Jones*, 958 F.2d 347 (Fed.Cir.1992); *Dillon*, 919 F.2d 688;*Grabiak*, 769 F.2d 729; *In re Lalu*, 747 F.2d 703 (Fed.Cir.1984)).
>
> [5] That test for prima facie obviousness for chemical compounds is consistent with the legal principles enunciated in *KSR*.[2] While the KSR Court rejected a rigid application of the teaching, suggestion, or motivation ("TSM") test in an obviousness inquiry, **the Court acknowledged the importance of identifying "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does" in an obviousness determination**. *KSR*, 127 S.Ct. at 1731. Moreover, the Court indicated that there is "no necessary inconsistency between the idea underlying the TSM test and the Graham analysis." *Id.* As long as the test is not applied as a "rigid and mandatory" formula, that test can provide "helpful insight" to an obviousness inquiry. *Id.* **Thus, in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound**.

[3] The skilled artisan reading the claims of any of the foregoing applications (alone or in combination with Xue et al.) would not have been led to modify the claims of any of the foregoing applications in the manner needed to arrive at the presently claimed compounds. Indeed, the necessary modifications are precluded by (and therefore not even encompassed by) the claims of any of the foregoing applications. In view of the foregoing, Applicants respectfully request withdrawal of the rejection.

[4] Claims 1-7 and 9 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7, 9, and 11 of USSN 11/744,659 (Office Action, page 10).

Claims 1-7 and 9 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7, 9, and 11 of USSN 11/744,677 (Office Action, page 10).

This is respectfully traversed.

Each of USSN 11/744,659 and USSN 11/744,677 is a **divisional** application that claims priority to the present application. Moreover, the presently pending claims in both USSN 11/744,659 and USSN 11/744,677 are directed to subject matter that: (i) was subject to restriction by the Office in the present application; and (ii) was not elected by Applicants for prosecution in the present application (i.e., withdrawn subject matter). As such, both applications should be shielded from obviousness-type double patenting by the safe harbor provided by 35 U.S.C. § 121. Applicants therefore request further clarification as to how *In re Schneller* supercedes this provision of 35 U.S.C. § 121.

The fee in the amount of $120 for the one month extension fee is being paid concurrently herewith on the Electronic Filing System (EFS) by way of a Deposit Account authorization. Please apply any other charges or credits to deposit account 06-1050, referencing Attorney Docket No. 06275-503US1.

Respectfully submitted,

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John T. Kendall, Ph.D.
Reg. No. 50,680

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110
Telephone: (617) 542-5070
Facsimile: (617) 542-8906

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